Application of Nutrigenomic Technologies to Personalize Nutrition

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Disclosure

- Nothing to disclose

Nutrigenomics: Out of the Lab and Into the Clinic

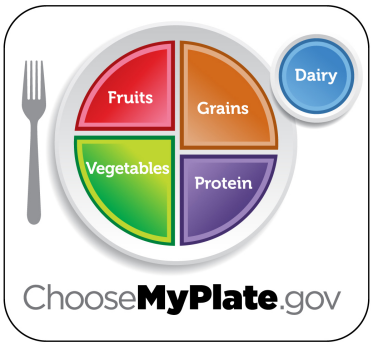
- Primer on Science of Nutrigenomics
- Why RDs Should be Aware of Nutrigenomics
- Clinical Application & Helpful "How-To" Tips
- Case Study Examples

In your experience as a practicing RD, does **'one-size-fits all'** approach to nutrition intervention work?

Scenario A

- Alex is a 27 y.o. young male professional
- Overweight, no significant PMH, normal labs
- Makes an appointment with RD for dietary advice
- **Chief Complaint:** Would like to 'get healthy'

Nutrition Prescription



Scenario A

- Alex returns 1 month later
- He feels he has more energy
- He has lost about 4#
- Brings in food diary and has been following MyPlate exactly as directed
- **Chief Complaint:** He documents gassiness, bloating, diarrhea, abdominal pain following each meal/snack containing fluid cow's milk

Does **'one-size-fits all'** approach work?

NO!

Lactose Intolerance

- Genetic condition where mutations or decreasing activity in the LCT gene necessary to produce lactase occur, leading to impaired ability to digest lactose.
- Because of the s/s – genetic test is typically not warranted

Why the Interest in Nutrigenomics?

Personalized Medicine

Personalized Medicine

FNCE 2014 Presidents Lecture - 'Personalized Medicine: The Changing Landscape of Health Care'

- *"Dietitians are part of a larger effort to integrate diet, nutrition, and metrics into personalized medicine. While research is limited in regards to wellness, prevention, and treatment, the movement to personalized medicine is growing exponentially."*
- *"Not only within the health care industry itself, the field of Individualized Medicine and the power that nutrigenomics brings, is also changing the way registered dietitian nutritionists think about the way they should interact and prepare for the future of health care."*

Personalized Medicine

*"Launched with a $215 million investment in the President's 2016 Budget, the Precision [Personalized] Medicine Initiative will pioneer a new model of **patient-powered research** that promises to accelerate biomedical discoveries and provide clinicians with new tools, knowledge, and therapies to select which treatments will work best for which patients."*

Fact Sheet: President Obama's State of the Union Address– Jan 30th, 2015

Tools to Personalize Medicine

- **Pharmacogenomics**
  - Uses an individual's genome to determine tailored drug prescription
- **Pharmacy compounding**
  - Creating more specific targeted drug and supplement therapies
- **Oncogenomics**
  - Application of genomics with cancer research and treatment
- **Preventive Care**
  - Screenings for BRCA1 and BRCA2 mutations with family hx of breast/ ovarian cancer

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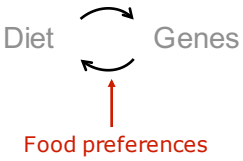
- **Nutrigenomics**
  - Prevent chronic disease by examining how the interaction between genes and diet can positively influence human health

PRIMER ON SCIENCE BEHIND NUTRIGENOMICS

The Science of Nutrigenomics

- Multidisciplinary science (nutrition + genomics) which studies how foods affect our genes and how individual genetic differences affect the way we respond to nutrients.



Scenario B

Husband and wife of 40 years

Eat the exact same 3 meals/ day

- Lean meat
- Non-starchy veggies
- Whole grain
- Low fat dairy
- Fruit

Exercise 6 hours/ week together

Wife:

- Cholesterol **<200mg/dL (nomal)**

Husband:

- Cholesterol **>250mg/dL (high)**

WHY?

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WHY?

Five Tenets of Nutrigenomics

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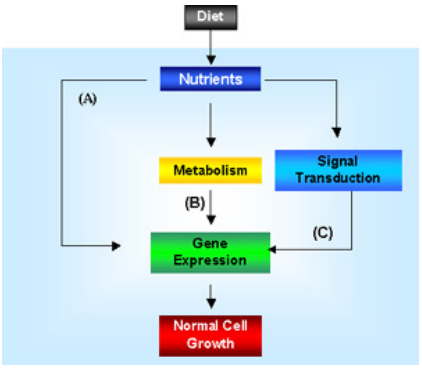
4. Some **diet-regulated genes** (and their normal, common variants) are likely to play a role in the onset, incidence, progression, and/or **severity of chronic diseases.**
5. **Dietary intervention** based on knowledge of nutritional requirement, nutritional status, and genotype (i.e., "**personalized nutrition**") **can be used to prevent, mitigate or cure chronic disease.**

Science of Nutrigenomics

Protein products of our genes *(enzymes, transporters, receptors, hormones, etc.)* interact with dietary components and influence our nutritional status

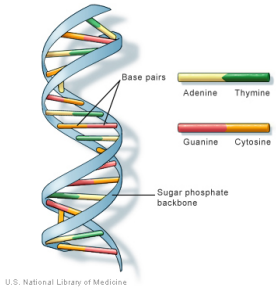
Humans are genetically very similar, but our genetic blueprints differ enough to set us apart from others.

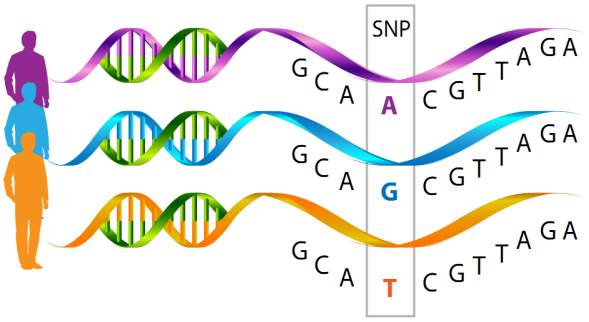
Single Nucleotide Polymorphisms (SNPs) – determine the different effects nutrients have on our bodies and how foods get metabolized.



The Science of Nutrigenomics

- Genes consist of sequences of 4 nucleotides
  - (A, C, G and T)
- >1 possible nucleotide at a given position
  - "C" replacing "A"
- Two copies of each gene are inherited
  - Three possible genotypes (AA, AC, CC)
- How do SNPs affect our risk of disease?

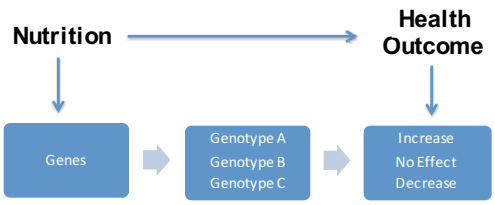




SNPs and Modifier Genes

- One gene, one disease → Not always the case
  - Cystic Fibrosis
  - Huntington's Disease
  - Phenylketonuria
- Modifier genes
  - Influence the expression of another gene
- This makes translating the science to practice more complex

Role of 'Modifier' Genes in Nutrition



One size does not fit all

WHY RDS SHOULD BE AWARE OF NUTRIGENOMICS

Why RDs Should be Aware of Nutrigenomics

- Genomic technologies → medicine of the future
- Utilize cutting edge resources available to you
- May increase visibility
- Stake your claim as the go-to expert in personalized nutrition
- Increases patient adherence to recommendations

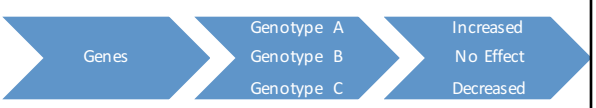
Nutrigenomics Research

Dietary Component	Genetic Component	Frequency of Variation	Optimal Intake	Associated Condition	% with suboptimal intake*
Vitamin C	GSTT1	20%	75-90 mg	CVD, DM II	**20%**
Folate	MTHFR	67%	400 mcg	CVD, stroke	**84%****
Whole Grains	TCF7L2	50%	100%	DM II	**n/a**
Omega-3	NOS3	50%	1.24 g	^TGs	**n/a**
Saturated Fat	APOA2	14%	<10% of T kcals	Obesity	**50%**
Sodium	ACE	70%	<1500 mg	HTN	**>90%**
Caffeine	CYP1A2	50%	<200 mg	MI, HTN	**n/a**
Gluten	HLA	30%	Varies	Celiac	**n/a**

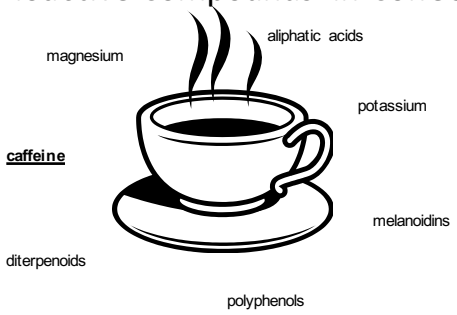
*Statistics Canada: Canadian Community Health Survey, Cycle 2.2
** Naturally occurring folate

Is Coffee Associated with CVD?

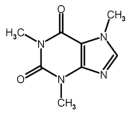
Coffee → CVD

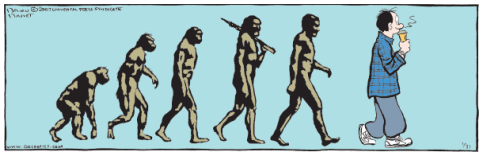


Bioactive Compounds in Coffee

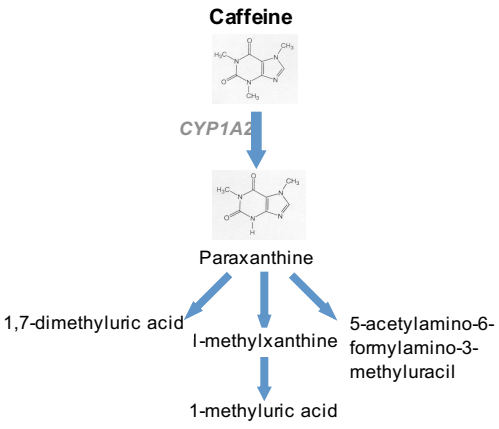


Caffeine (1,3,7-trimethylxanthine)

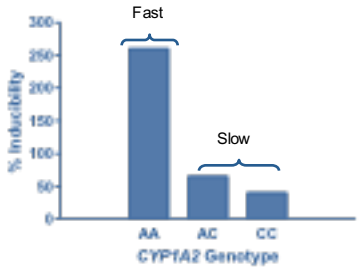




Caffeine



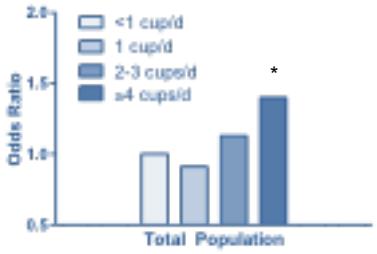
Genetic Variation in CYP1A2



Costa Rica Heart Study

- 2013 cases (myocardial infarction)
- 2013 population based controls
  - Matched (age, sex, area of residence)
- Data collection
  - FFQ
  - Health and lifestyle questionnaire
  - Fasting Blood Sample (DNA)

Coffee Intake and Risk of MI



* P<0.05

Cornelis *et al.*, JAMA 295: 1135-41, 2006

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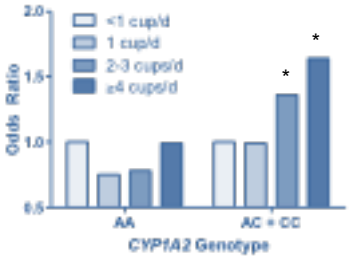

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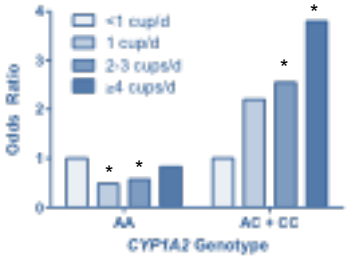
Coffee Intake and Risk of MI

Subjects <50 Years of Age



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Is Coffee Associated with CVD?

- Protective and pose and increased risk depending on the genetic variation of the CYP1A2 variant
- Personalized and tailored advice provided to patient to reduce risk

Why RDs Should be Aware of Nutrigenomics

Personalized Nutrition Expert

Journal of Nutrigenetics and Nutrigenomics

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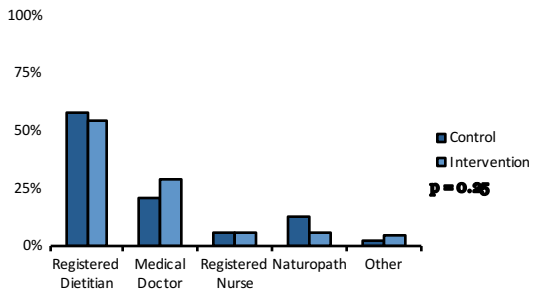
Original Paper

Perceptions of Genetic Testing for Personalized Nutrition: A Randomized Trial of DNA-Based Dietary Advice

Daiva E. Nielsen Sarah Shih Ahmed El-Sohemy

Department of Nutritional Sciences, University of Toronto, Toronto, Ont., Canada

Which group do you feel would provide you with the best personalized nutrition advice?



Within our Scope as Dietitians?

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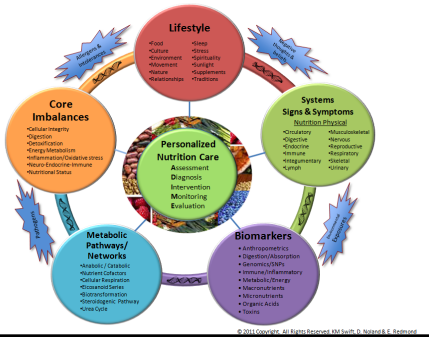
- We do not need to become chefs in order to teach people how to cook healthful meals.
- We do not have to be geneticists in order to practice Nutrigenomics.
- We are THE nutrition experts and the most trusted source of evidenced-based food and nutrition information, thus should be THE ONLY practitioners providing personalized nutrition advice.

Dietitians in Integrative & Functional Medicine (DIFM)

Integrative & Functional Medical Nutrition Therapy (IFMNT) Radial

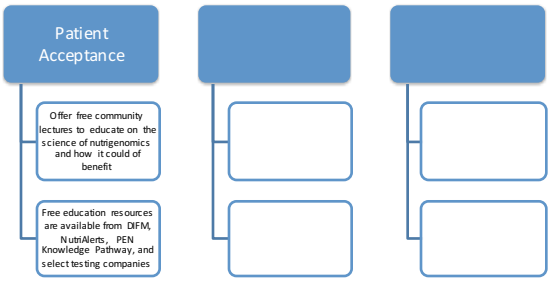


The Integrative and Functional Medicine Nutrition Therapy (IFMNT) Radial

- IFMNT Radial was established as an integrated conceptual framework to assist in IFMNT practice.
- The circular architecture of the IFMNT Radial allows for the evaluation of complex interactions and interrelationships.
- **The Radial depicts that food is a determining factor in health and disease and is a source of biological information that influences, and is influenced by, the five key areas.**
- The five key areas are: lifestyle, systems (signs and symptoms), core imbalances, metabolic pathways, and **biomarkers (i.e. Genomics and SNPs)**.
- Surrounding the Radial are precipitating factors that can affect the individual.

CLINICAL APPLICATION & HELPFUL "HOW-TO" TIPS

Preparing to Offer Nutrigenomics Testing



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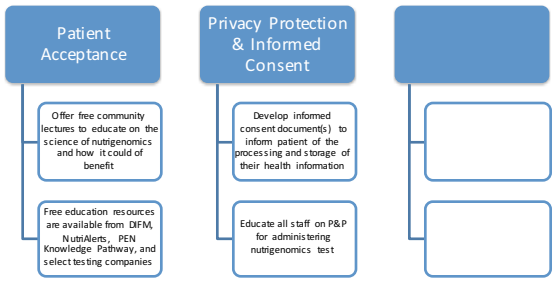

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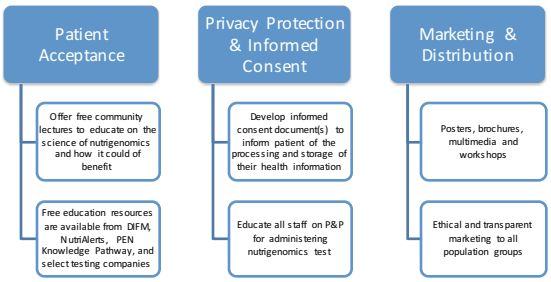


Packaging and Marketing your Services

- Special event pricing paired with informative workshop
- Included as part of multiple session package deal
- Included as part of testing in Executive Health Program
- Included as part of multiple week 'Healthy Living' course

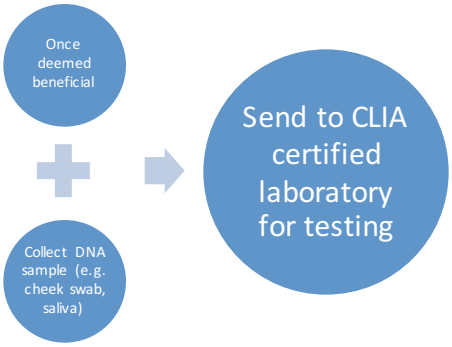
Nutrigenomics: Right for Every Patient?

- **Nutrition Assessment:**
  - Review and assessment of patient PMH and goals
  - Estimate nutrient intake (dietary recall, food journal, etc.)
  - Analysis of patient laboratory values and biometrics
  - Family health history; ethno-cultural risk
  - Assess readiness to change

Nutrigenomics: Right for Every Patient?

- **Is Nutrigenomics testing ethically relevant to this patient?**
  - Insurance coverage or Private Pay?
  - Money better spent on increased consumption of fruits and vegetables at this stage?
  - Is the client already adhering to stringent dietary recommendations?

Step 1: Administering a Genetic Test



Step 2: Translating the Results & Customizing a Dietary Plan	
• Present and interpret copy of results to patient	
• Each gene variant and associated dietary component discussed with patient based on risk (typical or elevated)	
• Dietary intervention tailored further based on patient's risk variant	
Examples:	
Pt. has 'elevated risk' for high blood pressure with a high sodium intake. *Pt. may benefit from decreasing sodium in diet.* *Dietary plan would include 1500-2300mg sodium.*	*'Typical risk' for heart disease without regards to caffeine intake.* *Pt. may not benefit from decreasing coffee intake (good source of antioxidants) to lower heart risk.* *Dietary plan would allow for ~4 cups of coffee equivalent caffeine per day.*

4 Approaches for Utilizing Nutrigenomics in Clinical Practice

CASE STUDIES

CASE STUDY MR. A

Mr. A: Nutrition Assessment

- 60 year old male
- Married, 2 adult children that live independently
- Executive Health Patient for 6 years
- Senior executive working 70+ hour weeks, just retired
- Osteoarthritis in knee: Scheduled for knee replacement surgery in May.
- Surgeon strongly recommended weight loss to reduce surgical complications

Mr. A: Nutrition Assessment & Diagnosis

1. Obesity
   - Weight: 226 pounds; BMI: 31.2
   - Waist Circumference 44.5 inches
2. NAFLD: Fatty Liver
   - Mildly elevated liver enzymes (ALT and AST)
   - Fatty liver observed on ultrasound
3. Heart Health
   - Borderline hypertension
   - Dyslipidemia
   - Framingham Risk Score Intermediate: 15.6%
   - Declining fitness: VO2 Max
     - Normal in 2008 (35.9 ml/kg/min)
     - Low in 2013- 7% of predicted (at 24.1 ml/kg/min)

Mr. A: Intervention

- 1-2 hour per week commitment for meetings with health care providers
- 12 visits with case manager
- 4 visits with each Wellness Provider: Dietitian, Psychologist and Exercise Physiologist
- Pre- and Post-testing: RMR, VO2 Max, Strength, ultrasound, DEXA Body Composition, BP, Blood work

Mr. A: Monitor and Evaluation

Follow Up Visit:

Eating plan & weight loss going well	2000-2300 Calories per day	Following DASH diet except for sodium restriction	BP improved but not optimal for surgery	Not fully motivated to make one more change, and neither is his wife, the family cook	Nutrigenomic testing conducted during this f/u visit

Mr. A: Nutrigenomics Testing:

Nutrigenomics Risk Variants:

Elevated risk for conditions related to intake of:

- Sodium
- Folate
- Whole Grains

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Nutrigenomics Risk Variants:

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Impact on Behavior Change:

- Mr. and Mrs. A. changed meal preparation so that no packaged and prepared foods are used.
- Mr. A tracks his food intake on MyNetDiary and he added folate (DFE) and sodium to his tracked list
- Added daily legumes for folate and limited sodium intake to <1500 mg per day within 2 weeks
- Improved consistency of optimal DASH dietary intakes

Mr. A: Monitor and Evaluation

Measures	January 2013	May 2013	May 2014
Weight / WC	226 lb / 44.5"	206 lb / 41.7"	205 lb / 41.5"
Blood Pressure	135/85	125/84	**117/72**
VO2 Max	24.1 ml/kg (7% of predicted)	34.4 ml/kg-min (90% of predicted)	31.0 ml/kg/min (82% of predicted)
DEXA Body Composition	36.2% fat 134.7 lbs lean RSMI: 8.19 kg/m2	32.6% fat 133.1 lbs lean RSMI: 7.57 km/m2	Not measured
RMR (Calories)	1817 (94% predicted)	1399 (70% predicted)	1802 (94% predicted)

*Without telling caregivers, Mr. A decided to reduce his daily calorie intake from 2000 to 1400 in the last two weeks of program. His goal was to lose more weight at the end. He slowed his rate of weight loss.

Mr. A: Monitor and Evaluation:

Sixteen Months After Nutrigenomic Testing:	
Sodium	**1350 mg***
Folate:	**142% of optimal intake***
Calories:	2050 kcal/day*
Blood Pressure:	**Lower than it has ever been (per pt.)**
Adherence to plan:	96% (per pt.)
Acceptance:	**Both pt. and wife report being very pleased with nutrigenomics testing. Sodium and folate are always top of mind.**
Newly adopted habits:	Soaking and cooking dried legumes and using daily
	Habitually eats a folate rich vegetables every lunch (100-150mcg) in salads and soups
	Grateful to know he had the typical variant for caffeine, along with all the other typical variants
Further Goals:	**Committed to increasing efforts to lose an additional 10# while still meeting folate and sodium needs**

*average daily intake

CASE STUDY: MS. B

Ms. B: Nutrition Assessment

- Ms. B is a 45 year old female lawyer, high achieving
- Patient has health anxiety and interested in genetic testing
- No metabolic health issues
- Diet already meets optimal intake for all nutrigenomics elevated risk recommendations
- Nutrigenomics education used to confirm that patient is making optimal choices, above and beyond standard guidelines and that testing does not benefit her at this time
- Patients lifestyle choices affirmed and she was encouraged to continue with optimal diet and no testing

CASE STUDY MR. C

Mr. C: Nutrition Assessment

- 54 y.o. male, married with 3 children
- EHP patient for 4 years
- Anthropometrics stable and appropriate, except 3 pound weight gain this year
  - (BMI=25 and WC=34.5")
- Strict Hindu vegetarian at home. Eats fish at work for heart health.
- Dyslipidemia (prior to statin treatment in 2010):
  - LDL –4.43 mmol/L
  - HDL - .91 mmol/L
  - TGs –3.33 mmol/L
- Blood Pressure: mildly elevated for 3 years – 129/88 mmHg

Mr. C: Nutrition Assessment

Goals

- Lose the 3 pounds he gained over previous summer
- Have diet that supports maintaining optimal LDL levels on statins (focused on no saturated fat)
- Live a long healthy life with no heart disease or stroke
- Reduce fish intake if he can (prefers Hindu vegetarian diet)

Mr. C: Nutrition Diagnosis

Diet history reveals high compliance Issue: suboptimal protein intake with heart healthy diet

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Diet history reveals high compliance Issue: suboptimal protein intake with heart healthy diet

- Patient replaced all ghee with olive oil or avocado oil to reduce saturated fat
- To reduce fat intake, patient rarely eats cheese or eggs
- Patient consumes > 15 g per day of soluble fiber
- Breakfast provides an average of 12 grams protein per day
- Dinner provides an average of 15 grams protein per day
- Average daily intake of protein is 0.8-1.0 g/kg/day

Mr. C: Nutrition Diagnosis

Diet history reveals high compliance Issue: suboptimal protein intake with heart healthy diet

- Patient replaced all ghee with olive oil or avocado oil to reduce saturated fat
- To reduce fat intake, patient rarely eats paneer or eggs
- Patient consumes > 15 g per day of soluble fiber from psyllium and legumes
- Breakfast provides an average of 12 grams protein per day
- Dinner provides an average of 15 grams protein per day
- Average daily intake of protein is 0.8-1.0 g/kg/day

- **Mr. B. is not comfortable adding cheese or eggs to his diet to ^ his protein intake.**
- **He is concerned about the saturated fat increasing his LDL cholesterol.**
- **He does not eat tofu and is not fond of Greek yogurt.**

Mr. C: Intervention

- **Increase protein intake**
- Use Nutrigenomics testing to encourage Mr. B to allow 7% of his daily calorie intake to come from saturated fat (15 grams per day)

Goal

Mr. C: Intervention

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Goal

Negotiation 1:

- **If his nutrigenomic test for saturated fat is "typical"**, Mr. B will allow 5 grams of saturated fat to be added to his diet per day (so 2 eggs or ~2 oz of low fat cheese), providing 12 grams of added protein per day

Mr. C: Intervention

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Negotiation 1:

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- **If the nutrigenomic test for omega-3 fats is elevated**, he will continue to eat fish every day, otherwise he will reduce fish to twice per week and find an alternate protein source at lunch

Negotiation 2:

Mr. C: Nutrigenomics Testing

Nutrigenomics Risk Variants

Elevated risk for conditions related to intake of:

- Sodium
- Omega-3 Fat

Mr. C: Nutrigenomics Testing

Nutrigenomics Risk Variants

Elevated risk for conditions related to intake of:

- Sodium
- Omega-3 Fat

Mr. B accepting of negotiated choices and willing to adhere to recommendations

- Sodium intake was already < 1500 mg per day
- **Patient will continue to eat fish every day at lunch**
- Patient had switched from regular to Greek yogurt at breakfast
- **Patient is now confident eating some saturated fat and is willing to add cheese or egg to his dinner meal to increase protein intake**
- Blood work lipid panel will be repeated in 3 months
- **If lipids worsen, Mr. B agreed to be open to tofu**
- Body Composition Testing Completed to get baseline lean muscle mass.

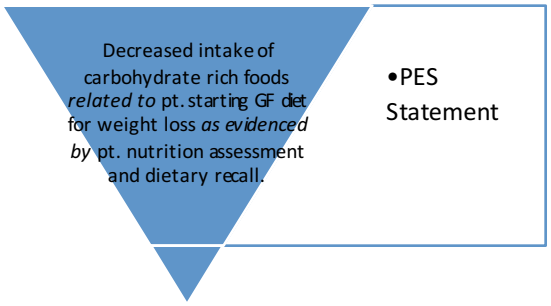
*Monitoring and Evaluation of Intervention is underway
*Used as a tool to negotiate and prioritize dietary modifications

CASE STUDY MS. D

Ms. D Nutrition Assessment

- 25 y.o. female
- BMI: 28
- Good physical health
- Negative family history for Celiac Disease
- Has adopted gluten free diet for weight loss
- Dietary recall reveals minimal intake of whole grains and dietary fiber
- Pt. states she has low energy and irregular BM

Ms. D Nutritional Diagnosis



Ms. D Intervention

Pt. educated on the evidenced based research regarding gluten containing foods and dangers associated with fad diets	Pt. provided with education on genetic test to possibly 'rule out' Celiac Disease	Pt. currently following GF diet, thus blood test may not be accurate	Pt. decides to undergo nutrigenomic testing for CD risk

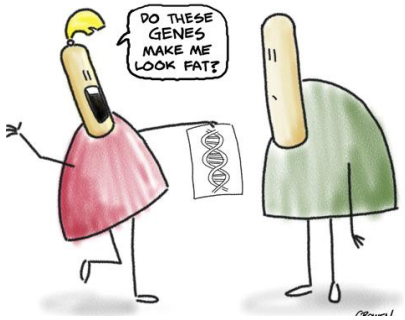
Ms. D Monitor & Evaluate:	Pt. genetic test results suggest 'low risk' for CD
	Pt. decides to adhere less strictly to GF dietary recommendations.
	She began including more whole grain, nutrient dense foods (both gluten containing and non-gluten containing.)
	Pt. reports having more energy, improved BM and better understanding of importance of maintaining a balanced diet while reducing overall calories for sensible and sustained weight loss.

Closing Summary

- Primer on the Science of Nutrigenomics
- Why RDs Should be Aware of Nutrigenomics
- Clinical Application & Helpful "How-To" Tips
- Discussed Case Study Examples

Ready to Learn More?

- Graduate and undergraduate courses at colleges and universities
  - Textbooks on DIMF website
- Penn State Center for Excellence in Nutrigenomics
- Medical News Today: Genetics News
- Journal of Human Genetics
- International Society of Nutrigenetics and Nutrigenomics
  - 20% discount to DIFM members
- Genetic Testing Companies-
  - List of companies on DIFM website
- Practice Based Evidence in Nutrition (PEN)
  - *Knowledge Pathway on Nutrigenomics*
- UC Davis: Online Nutrigenomics Course
- Nutrigenomics Organisation: *NutriAlerts*



Thank You

QUESTIONS?